

## REMARKS

Claims 1-28 and 36-38 were pending and presented for examination and in this application. In an Office Action dated August 7, 2008, claims 7, 14 and 15 were objected to, and claims 1-6, 8-11 and 16-23 were rejected. Applicant thanks Examiner for examination of the claims pending in this application and for pointing out the allowable subject matter. Applicant addresses Examiner's comments below.

In view of the Remarks that follow, Applicant respectfully requests that Examiner reconsider all outstanding objections and rejections, and withdraw them.

### **Response to Rejection Under 35 USC 103(a)**

In the 3rd paragraph of the Office Action, Examiner rejects claims 1-6, 8-11, and 16-23 under 35 USC § 103(a) as allegedly being unpatentable over Alizadeh et al. (Nature (2000) Volume 403, pages 503-511) ("Alizadeh") in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991) ("Bertucci"). This rejection is respectfully traversed.

The references cited by the Examiner do not disclose all of the elements of the claims. The Examiner contends that Alizadeh discloses "a first reference set of genes," "a second reference set of expressed genes independent of the first reference set from a third and fourth sample where the third or fourth sample is from a different source than the first and second sample," and "identifying a concordance set of expressed genes." Applicant respectfully disagrees.

Alizadeh discloses characterizing gene expression patterns for 96 normal and malignant lymphocyte samples with cDNA microarray analysis (“First Analysis”). Alizadeh analyzes the results of this analysis with a hierarchical clustering algorithm. Alizadeh at 504, col. 1, last paragraph. This algorithm results in several clusters. This experiment could be analogous to identifying a first reference set of expressed genes.

There is however then no further identification of a “second reference set of expressed genes that includes at least one gene that is not included in the first reference set, said second reference set consisting of genes that are differentially expressed between a third sample and a fourth sample, at least one of which originates from a different source than said first and second samples.” The portion of Alizadeh cited by the Examiner as disclosing the “second reference set of expressed genes,” “Analysis of gene expression in lymphoid malignancies” on page 504, is discussion of the clustering found with the hierarchical clustering algorithm of the First Analysis. There are no samples other than the 96 that were originally analyzed and the data is from the First Analysis.

Alizadeh goes on to disclose additional discussions of expression data but all are of the data resulting from the First Analysis. Alizadeh discloses reclustering of the data from the First Analysis using just the diffuse large B-cell lymphoma (“DLBCL”) cases that were part of the original 96 samples. This reclustering shows differentiation between germinal centre B-like DLBCL (“GC B-like DLBCL”) and activated B-like DLBCL. None of these samples however originate “from a different source than said first and second samples” because those same DLBCL cases, both GC B-like DLBCL and activated B-like DLBCL, were part of the malignant lymphocyte samples of the First Analysis.

The problem existing in the art which the claimed invention alleviates is not solved by the method disclosed by Alizadeh. Because of the heterogeneity of cells, identifying genes are differentially expressed in tumors and are also useful for prognosing tumors has traditionally been difficult. Instant Application, par [0006]. The claimed invention is a biologically-based solution to this problem by utilizing cells from different sources to be able to focus on those that are biologically most important. Alizadeh does not disclose using samples from different sources and therefore does not solve the problem of identifying genes that would be useful for prognosing samples other than those which were initially tested.

With regard to the second reference, Bertucci, the Examiner maintains that Bertucci discloses “a first correlation coefficient, correlating for said genes within said subset a first expression differential between said first and second samples to a second expression differential between third and fourth samples, exceeds a predetermined value.” The Examiner points to the bottom paragraph of the right column of page 2987 of Bertucci as disclosing a correlation coefficient that correlates for a differential between the first and second samples and a differential between the third and fourth sample. As the Examiner pointed out, Bertucci discloses, “correlations of gene pairs based on expression profiles were measured with the correlation coefficient,  $r$ .” This discloses a correlation coefficient for a pair of genes, not for two expression differentials, the first between a first and second sample and the second between a third and fourth sample. Therefore Bertucci does not disclose the correlation coefficients of the claimed invention.

Accordingly, the combination of Alizadeh and Bertucci fails to teach all of the elements of claim 1, and so cannot render independent claim 1 obvious, nor the claims that depend

therefrom (claims 2-23). Therefore withdrawal of this ground of rejection is respectfully requested.

Claims 12 and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Alizadeh et al. in view of Bertucci et al. and further in view of Young et al. (US Publication No. 2005/0255588 A1). Claims 12 and 13 depend from and incorporate all of the elements of claim 1. Therefore, claims 12 and 13 cannot be rendered obvious by the cited art for at least the reasons described above regarding claim 1. Accordingly, Applicant requests withdrawal of this rejection of claims 12 and 13.

Claims 24-28 and 36-38 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Alizadeh et al. in view of Bertucci et al. and further in view of in view of Horne et al. (U.S. Patent No. 6,974,667) (“Horne”) in view of Dai et al. (U.S. Patent No. 7,171,311) (“Dai”) in view of Ohara et al. (DNA Res. (1997) Volume 4, number 5, pages 345-349) (“Ohara 1”) in view of Bach (Nucleic Acids Research (1991) Volume 19, number 13, pages 3553-3559) (“Bach”) in view of Volta et al. (Genomics (1999) Volume 55, number 1, pages 68-77) (“Volta”) in view of Ohara et al. (DNA Res. (1998) Volume 5, number 3, pages 169-176) (“Ohara 2”) in view of Venter et al. (U.S. Patent No. 6,812,339) in view of Calabretta et al. (U.S. Patent No. 5,734,039) (“Calabretta”), in view of Wohlgemuth et al. (U.S. Patent No. 6,905,827) (“Wohlgemuth”), in view of Cocks et al. (U.S. Patent No. 6,607,879) (“Cocks”). Claims 24-28 and 36-38 depend from and incorporate all of the elements of claim 1. Therefore, claims 24-28 and 36-38 cannot be rendered obvious by the cited art for at least the reasons described above regarding claim 1. Accordingly, Applicant requests withdrawal of this rejection of claims 24-28 and 36-38.

Based on the above remarks, Applicant respectfully submits that for at least these reasons claims 1-6, 8-11, 16-28 and 36-38 are patentably distinguishable over the cited reference. Therefore, Applicant respectfully requests that Examiner reconsider the rejection, and withdraw it.

**Conclusion**

In sum, Applicant respectfully submits that claims 1-6, 8-11, 16-28 and 36-38, as presented herein, are patentably distinguishable over the cited references (including references cited, but not applied). Therefore, Applicant requests reconsideration of the basis for the rejections to these claims and request allowance of them.

In addition, Applicant respectfully invites Examiner to contact Applicant's representative at the number provided below if Examiner believes it will help expedite furtherance of this application.

Respectfully Submitted,  
Guennadi V. Glinskii

Date: 6 November 2008

By: /Pauline Farmer-Koppenol/

Pauline Farmer-Koppenol, Reg. No. 58,004  
Fenwick & West LLP  
Silicon Valley Center  
801 California Street  
Mountain View, CA 94041  
Tel. (650) 335-7181  
Fax (650) 938-5200